Diagnostic criteria for drug rash and eosinophilia with systemic symptoms

Dear Editor,

We found the paper by Jmeian *et al.* concerning a case of allopurinol-related drug rash with eosinophilia and systemic symptoms (DRESS) in a patient of chronic kidney disease and gout, interesting.[1] The presence of eosinophilia, the temporal relationship of the symptoms with the initiation of treatment with allopurinol, and the marked improvement on withdrawal of the drug along with the administration of systemic corticosteroids were features suggesting the diagnosis of DRESS.

DRESS is considered a severe drug reaction with a case fatality rate of 10–20%.[2] The diagnosis is sometimes difficult since the clinical manifestations may be incomplete or nonspecific, and it can also present as a purely systemic disease without any cutaneous involvement.[3,4]

Multiple diagnostic criteria have been developed and used to standardize the diagnosis and management of DRESS, albeit with limited success.

Bocquet *et al.* were the first who proposed criteria for DRESS [Table 1].[5] The Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) group suggested criteria for hospitalized patients with a drug rash to diagnose DRESS syndrome [Table 2].[6] RegiSCAR constitutes a European RegiSCAR, including Stevens–Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and DRESS. In an effort to define more accurately the DRESS syndrome, a scoring system has also been developed the RegiSCAR scoring system [Table 3].[6] A Japanese group suggested another set of diagnostic criteria; however, universal adaptation of this criteria may be limited since one of the criteria includes HHV-6 activation and some tests, such as measurement of IgG titer anti-HHV 6, are yet not routinely available [Table 4].[7]

DRESS is a challenging drug adverse reaction which can cause life-threatening organ dysfunction. Clinicians must be alert to this possibility to reach the correct diagnosis and institute the appropriate management.

Table 1: Bocquet *et al.* proposed criteria for diagnosis of drug rash and eosinophilia with systemic symptoms/ drug-induced hypersensitivity

DRESS is confirmed by the presence of 1 and 2 and 3
Cutaneous drug eruption
Adenopathy >2 cm in diameter or hepatitis (liver transaminases >2 times of normal or interstitial nephritis or interstitial pneumonia or carditis
Hematologic abnormalities eosinophilia >1.5×10^9/L or atypical lymphocytes

DRESS: Drug rash and eosinophilia with systemic symptoms

Table 2: Registry of severe cutaneous adverse reaction criteria for diagnosis of drug rash and eosinophilia with systemic symptoms

1. Hospitalization*
2. Reaction suspected to be drug-related*
3. Acute rash*
4. Fever >38°C†
5. Enlarged lymph nodes at a minimum of 2 sites†
6. Involvement of at least 1 internal organ†
7. Blood count abnormalities†
Lymphocytes above or below normal limits
Eosinophils above the laboratory limits
Platelets below the laboratory limits

*Necessary criteria are required for making the diagnosis. †Three out of four criteria are required

Table 3: Registry of severe cutaneous adverse reaction diagnosis score for drug rash and eosinophilia with systemic symptoms

Features	No	Yes	Unknown
Fever >38.5°C	−1	0	−1
Enlarged lymph nodes (>2 sites, >1 cm)	0	1	0
Atypical lymphocytes	0	1	0
Eosinophilia			0
700-1499 or 10%-19.9%	0	1	
≥1500 or ≥20%		2	
Skin rash			
Extent >50%	0	1	
At least 2: Edema, infiltration, purpura, scaling	−1	1	
Biopsy suggesting DRESS	−1	0	
Internal organ involvement			
One	0	1	0
Two or more		2	
Resolution in ≥15 days	−1	0	−1
Evaluation of other potential causes (antinuclear antibody, blood culture, serology for HAV/HBV/ HCV, chlamydia/mycoplasma)	0	1	0
If none of these positive and >3 are negative			

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Conflicts of interest

There are no conflicts of interest.

Table 4: Japanese group's criteria for diagnosis of drug rash and eosinophilia with systemic symptoms/ drug-induced hypersensitivity

1. Maculopapular rash developing >3 weeks after starting with the suspected drug
2. Prolonged clinical symptoms 2 weeks after discontinuation of the suspected drug
3. Fever >38°C
4. Liver abnormalities (alanine aminotransferase >100U/L)*
5. Leucocyte abnormalities (at least one present)
   (a) Leucocytosis (>11×109/L)
   (b) Atypical lymphocytosis (>5%)
   (c) Eosinophilia (>1.5×109 /L)
6. Lymphadenopathy
7. Human Herpes 6 reactivation

The diagnosis is confirmed by the presence of the 7 criteria (typical DIHS) or of the five (1-5) (atypical DIHS). *This can be replaced by other organ involvement, such as renal involvement

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